REMARKS

Reconsideration of this application is respectfully requested.

Status of the Claims:

Claims 1-40, 43 and 44 are pending in this application. Claim 1 has been amended, *supra*, without admission and without prejudice to Applicants' right to pursue any subject matter that may have been surrendered by this amendment in either this or other (*e.g.*, related divisional and/or other continuing) applications. Specifically, claim 1 has been amended to specify that the method includes "cold micro-filtrating at the temperature which is sufficient to precipitate all the dissolved PHA." Claim 1 has also been amended to recite that "the cellular biomass is a biomass coming from any microorganism or plant, which is able to produce PHA naturally or by genetic modification, in order to render it a PHA producer or a high PHA producer." Support for these amendments is found throughout the application as filed, for example at pages 15 and 26. No new matter has been added to the application. Upon entry of these amendments, claims 1-40, 43 and 44 will remain pending and under consideration. Entry and consideration of these amendments is respectfully requested.

Rejection under 35 U.S.C. § 102/103:

Claims 1-40, 43 and 44 have been rejected under 35 U.S.C. § 102(b) as anticipated by, or alternatively, under 25 U.S.C. § 103(a) as obvious over U.S. Patent Nos. 6,323,276 ("Horowitz I"), 6,228,934 ("Horowitz II"), 6,368,836 ("Horowitz III"), 4,968,611 ("Traussnig"), and 5,213,976 ("Blauhut"). According to the Examiner, it would have been obvious to perform the same process steps, or make routine optimizations thereof, to recover the claimed polyhydroxyalkanoate (PHA) species recited in the claims. The Examiner also cites numerous secondary references[1] which are said to teach isolation of the PHA species.

This rejection is traversed and reconsideration is respectfully requested.

[1] In the Office Action, the Examiner has cited, but not relied upon, the following references: U.S. Patent Nos. 6,410,096 (Eggink I); 5,958,480 ("EgginkII"); 5,942,597 ("Noda I"); 5,821,299 (NodaII); and 5,536,419 ("Escalona").

In the Office Action, the Examiner alleges that the claims are very complex, not allowing a clear understanding of the advantages over the state of the art. The Examiner further states that it would have been obvious for the skilled person to "follow the same steps, or make optimizations thereof (solution, solvents, amounts/ranges of materials used, etc.) to recovere [*sic*] the polyhydroxyalkanoate (PHA) species products of specifically poly-3-hydroxybutyrate (PHB) and/or poly(hydroxybutyrate-cohydroxyvalerate) (PHBV) in any of Horowitz et al. I-III, Traussing et al., or Blauhut et al., because each of the references advantageously teach the same or routinely optimizable steps of recovering the same polyhydroxyalkanoate (PHA) species of products." Office Action at pages 16-17.

However, as described in detail below, the specific process steps recited in the claims provide important and unexpected advantages for efficient and industrial-scale production of PHAs. Even if, *arguendo*, the individual steps set forth in the claims were already ***independently*** disclosed in the art, the particular sequence of these steps specified in the claims interact in a novel and non-obvious manner resulting in a high industrial efficiency (above 95%) and high-quality product (molecular weight of at minimum of 750,000 kDa and purity equal or higher than 99%).

Specifically, in the claimed process, the biomass is first concentrated through decantation. This concentration step contributes to the isolation of a quality end product not obtained using methods disclosed in any of Horowitz I, Horowitz II, Horowitz III, Traussnig or Blauhut. Further, this concentration step provides a high consistency, heavy and very stable biomass flake, which permits the initial removal of impurities through simple washing with water (dilution and re-concentration). The structural stability of the flakes produced in this step persist during the phases of adding the solvent, heating, agitating and extracting the PHA allowing the biomass residues to remain aggregated. These biomass residues consisting of heavy flakes, can be easily removed by applying low centrifugal force, *e.g.* by using hydrocyclones, and is very simple, cheap and of low maintenance. The use of filters is also facilitated due to the size of the residual biomass flakes, which are an aggregation of cells but thousands of times bigger than the original cells.

The methods used in Traussing and Noda require use of a cell concentration step by centrifugation. There is no mention of the flocculation step used in the pending claims. On the industrial scale, the use of centrifuges, without the resource of flocculation, is not practical and represents a very expensive alternative. Applicants discovered that cell flocculation allows one to carry out product concentration and separation using decanters, which is more practical on an industrial scale and cheaper than centrifugation. Applicants also discovered that the sole use of centrifugation for the concentration of

the cells, as disclosed in the prior art, produces cell populations that remain isolated, not having any synergistic effect on the other steps of the process mentioned above.

Another central aspect of the inventive process defined by the present claims is that the biomass suspension can be rapidly heated with the solvent. Applicants discovered that a very rapid heating of the humid biomass, reduces the exposure time of the polymer to high temperatures and produces a synergistically quicker rupture of the cell, making this entire step more efficient and less harmful to the polymer. This effect is obtained by injecting the solvent in the vapor phase jointly with an additional complement of pre-heated solvent into the biomass slurry, as set forth in the claims. This process allows for the use of non-toxic solvents, from renewable sources that are readily available. These solvents do not use precipitating agents to recover the dissolved polymer since the process of the pending claims provides a temperature-based means for precipitating the polymer. This process is particularly advantageous because it avoids carrying out the extraction process at high temperatures, which can cause damage to the polymer.

Further, the inventive method's combined use of hydrocyclones, filters and membranes, allows for the isolation of a polymer solution that is exceedingly pure, free of all biomass in a short period of time, minimizing the harmful effects of high temperatures. Immediately after removing the biomass, the polymer solution is cooled so as to precipitate the entire dissolved polymer. The claims specify an innovative means of using of using membrane filters to remove part of the solvent, which increases the concentration of polymer in the suspension. The membrane concentration also allows for the reduction of colored material dissolved in the solvent in contact with the polymer, which is of fundamental importance for the reduction of color of the polymer in the subsequent steps of purification.

In the removal of the solvent, after precipitation of the polymer, the claims recite an innovative set of steps, which produce polymer granules of high purity and molecular weight. First, the suspension is heated in water, so that most of the solvent forms a stream, which evaporates at low temperature resulting in the aggregation of the polymer into granules. At a specific point, these granules are ruptured through high shearing agitation, removing impurities and the residual solvent, yielding polymer particles of high purity, which are subsequently dried. This feature of granule formation and the effect of purification obtained by rupturing the granules which are large, porous and easily ruptured is not described in any of the references cited by the Examiner, and represents a significant advancement in the field.

The Blauhut reference discloses a complex and impractical means for obtaining the polymer product in high yield. In particular, Blauhut teaches long extraction periods, which cause damage to the polymer, along with very intense mechanical agitation which alters the molecular weight of the polymer.

The Blauhut methods do not allow for high yield of production and high quality of the end polymer (especially in relation to the molecular weight) as attained using the claimed method.

Horowitz I and Horowitz II describe processes for post-treatment of PHAs, which yield less crystalline material. The specific sequence of process steps set forth in the present claims is neither disclosed nor suggested in Horowitz I or Horowitz II. Further, Horowitz III describes a specific process of purifying PHAs which begins with material extracted from cells of microorganisms using an extraction process that is outside the scope of the pending claims. In particular the Horowitz III method uses diafiltration, which could not be applied in the industrial scale.

Moreover, the secondary references relied upon by the Examiner fail to disclose any of the unique method steps recited in the claims. In particular, Eggink I and Eggink II relate to methods for isolating an edible PHA suspension to be used in the protection of foodstuff. The processes of extraction/purification, described in these references, make intensive use of enzymes, which cannot be recycled. These references fail to disclose any of the method steps set forth in the pending claims.

The Escalona reference uses a technique very specific to halophilic microorganisms, this technique cannot be applied to other types of microorganisms, since the simple reduction of osmotic pressure by dilution is not enough to rupture the cell walls of most microorganisms. Further, the Escalona process produces an excessive amount of liquid residues and does not allow the recycling of products used in the extraction/purification of the polymers.

Noda discloses a process for purifying PHAs from oleaginous plants containing both vegetable oils as well as PHA, and is drawn to the separation of oil from the PHA which is not relevant to the present invention.

Finally, the claimed process has several advantageous features, not achieved in any of the references cited by the Examiner. In particular, the inventive method allows for use of low toxic solvents and is particularly efficient in liquefying PHB and PHB-HV. The method of the pending claims also uses a flocculation step, wherein heavy and stable biomass granules are aggregated, which allows re-purification through washing. The claimed method also provides a more efficient and rapid separation of the cellular debris by means of filters and hydrocylones. The use of microfiltration membranes allows for the rapid separation and recovery of part of the solvent. The process of granulation of the extracted PHA set forth in the claims provides a rapid and efficient separation of the remaining solvent and an excellent removal of the contaminated material adhering to the PHA. All of these features are ideal for industrial-scale isolation of PHAs. In addition to producing a high quality product, the method called for in the

pending claims is efficient and high yielding, not only in terms of energy consumption, but also safety, residues generated and costs of production.

For at least the foregoing reasons, claims 1-40, 43 and 44 are not anticipated and/or obvious over any of the cited references. Withdrawal of these rejections is respectfully requested.

Conclusion:

For at least the foregoing reasons, Applicants respectfully submit that each of the outstanding rejections to this application have been overcome and that the application is in condition for allowance. Accordingly, withdrawal of all rejections and allowance of the pending claims is repsectully requested. The Examiner is moreover invited to contact Applicants' undersigned representative should (s)he conclude that there are additional issues that could be readily resolved, *e.g.*, in an interview or by Examiner's Amendment. An allowance is earnestly sought.

Respectfully submitted,

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